

I claim:

Subst. A1

1. A cDNA gene encoding for receptor protein 4-1BB.
- 5 2. The cDNA gene of claim 1 having a nucleotide sequence as shown in Figures 2a and 2b.
3. A cDNA gene of claim 1, identified as p4-1BB deposited at the American Type Culture Collection at 12301 Parklawn Drive, Rockville, Maryland 20852 under 10 ATCC No.: 67825.
4. The cDNA of claim 2 and fragments and derivatives thereof, wherein said fragments and derivatives can be used as a probe to isolate DNA sequences encoding for proteins similar to the receptor protein encoded by said cDNA.
- 15 5. The cDNA of a human receptor corresponding to the mouse cDNA 4-1BB isolated from a human source using cDNA 4-1BB as a probe.
6. The receptor protein 4-1BB produced by
 - 20 a) inserting the cDNA of 4-1BB into an appropriate expression vector,
 - b) transfecting said expression vector into an appropriate transfection host,
 - c) growing said transfected hosts in appropriate culture media and
 - d) purifying the receptor protein from said culture media.
- 25 7. A protein having the amino acid sequence shown in figures 2a and 2b.
8. The protein of claim 7 and fragments and derivatives thereof, wherein said fragments and derivatives:
 - 30 a) can be used as a probe to isolate ligands to receptor protein 4-1BB;
 - b) can be used to stimulate proliferation B-cell's expressing 4-1BB ligands; or
 - c) can be used to block 4-1BB ligand binding.

9. A monoclonal antibody against 4-1BB which specifically recognizes an epitope on the extracellular domain of receptor protein 4-1BB.

10. The monoclonal antibody of claim 9 wherein said monoclonal antibody is produced from a hybridoma identified as 53A2 and deposited at the American Type Culture Collection at 12301 Parklawn Drive, Rockville, Maryland 20852 under ATCC No.: HB-11248.

11. A hybridoma capable of producing a monoclonal antibody against 4-1BB which specifically recognizes an epitope on the extracellular domain of receptor protein 4-1BB.

12. The hybridoma of claim 11 wherein said hybridoma is identified as 53A2 and deposited at the American Type Culture Collection at 12301 Parklawn Drive, Rockville, Maryland 20852 under ATCC No.: HB-11248.

13. The method of using the monoclonal antibody of claim 9 to enhance T-cell proliferation comprising the step of treating T-cells that have expressed receptor protein 4-1BB with said monoclonal antibody.

14. The method of claim 13 further comprising the step of conducting said treatment in the presence of protein tyrosinase kinase.

15. The method of using the monoclonal antibody of claim 9 to enhance T-cell activation comprising the step of treating T-cells that have expressed receptor protein 4-1BB with said monoclonal antibody.

16. The method of claim 15 further comprising the step of conducting said treatment in the presence of protein tyrosinase kinase.

17. A fusion protein for detecting cell membrane ligands to receptor protein 4-1BB, comprising:

5 a) at least a portion of said receptor protein 4-1BB corresponding to the extracellular portion of said receptor protein 4-1BB such that said portion of said receptor protein 4-1BB binds to said cell membrane ligands; and
b) a detection protein bound to said portion of said receptor protein 4-1BB such that ligand binding can be detected by relative activity assays for said detection protein.

10 18. The fusion protein of claim 17 wherein said detection protein is alkaline phosphatase.

15 19. A method of detecting cell membrane ligands to receptor protein 4-1BB, comprising:
a) providing a fusion protein including:
1) at least a portion of said receptor protein 4-1BB corresponding to the extracellular portion of said receptor protein 4-1BB such that said portion of said receptor protein 4-1BB binds to said cell membrane ligands, and
2) a detection protein bound to said portion of said receptor protein 4-1BB such that ligand binding can be detected by relative activity assays for said detection protein;
b) placing said fusion protein in the presence of a cell suspected to express said receptor protein 4-1BB;
c) washing said cell of any fusion protein not bound to said cell membrane ligands;
d) placing said washed cells in the presence of a substrate for said detection protein and measuring the relative activity of said detection protein.

20 20. The method of claim 19 wherein said detection protein is alkaline phosphatase.

25 21. A method of inducing B-cell proliferation comprising the step of treating B-cells that have expressed a ligand to receptor protein 4-1BB with cells that have expressed receptor protein 4-1BB.

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